# IARC MONOGRAPHS
# ON THE
# EVALUATION OF THE CARCINOGENIC RISK
# OF CHEMICALS TO HUMANS:

## Some *N*-Nitroso Compounds

Volume 17

This publication represents the views and expert opinions
of an IARC Working Group on the
Evaluation of the Carcinogenic Risk of Chemicals to Humans
which met in Lyon,
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IARC MONOGRAPHS

In 1971, the International Agency for Research on Cancer (IARC) initiated a programme on the evaluation of the carcinogenic risk of chemicals to humans involving the production of critically evaluated monographs on individual chemicals.

The role of the monograph programme is to collect all available relevant experimental and epidemiological data about groups of chemicals to which humans are known to be exposed, to evaluate these data in terms of human risk with the help of international working groups of acknowledged experts in chemical carcinogenesis and related fields, and to publish and disseminate the conclusions of those working groups as a series of IARC Monographs.



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## NOTE TO THE READER

The term 'carcinogenic risk' in the IARC Monograph series is taken to mean the probability that exposure to the chemical will lead to cancer in humans.

Inclusion of a chemical in the monographs does not imply that it is a carcinogen, only that the published data have been examined. Equally, the fact that a chemical has not yet been evaluated in a monograph does not mean that it is not carcinogenic.

Anyone who is aware of published data that may alter the evaluation of the carcinogenic risk of a chemical for humans is encouraged to make this information available to the Unit of Chemical Carcinogenesis, International Agency for Research on Cancer, Lyon, France, in order that the chemical may be considered for reevaluation by a future Working Group.

Although every effort is made to prepare the monographs as accurately as possible, mistakes may occur. Readers are requested to communicate any errors to the Unit of Chemical Carcinogenesis, so that corrections can be reported in future volumes.

### 3.3 Case reports and epidemiological studies

No data were available to the Working Group.

## 4. Summary of Data Reported and Evaluation

### 4.1 Experimental data

*N*-Nitrosodiethylamine is carcinogenic in all animal species tested: mice, rats, Syrian golden, Chinese and European hamsters, guinea-pigs, rabbits, dogs, gerbils, pigs, monkeys, hedgehogs, various fish, frogs and birds. It induces benign and malignant tumours after its administration by various routes, including ingestion, parenteral injection, inhalation and rectal instillation. The major target organs are the liver, respiratory and upper digestive tracts and kidney. It is carcinogenic following its administration prenatally and in single doses. In several studies, dose-response relationships were established.

*N*-Nitroso-*N*-ethyl-*N*-(2-hydroxyethyl)amine, a metabolite of *N*-nitrosodiethylamine, produced mainly liver tumours after its oral administration to rats.

### 4.2 Human data

No case reports or epidemiological studies were available to the Working Group. Available information on occurrence suggests that the general population may be exposed to low levels of *N*-nitrosodiethylamine; however, no exposed group suitable for an epidemiological investigation has yet been identified.

### 4.3 Evaluation

There is *sufficient evidence* of a carcinogenic effect of *N*-nitrosodiethylamine in many experimental animal species. Although no epidemiological data were available, *N*-nitrosodiethylamine should be regarded for practical purposes as if it were carcinogenic to humans.

(b) Humans

In 4 men, laboratory exposure to NDMA gave rise to acute liver necrosis which later developed into cirrhosis; in one case, the acute liver injury proved to be fatal (Barnes & Magee, 1954; Freund, 1937).

Studies *in vitro* suggest that NDMA is metabolized by human liver and lung *via* the same metabolic pathway as in other mammalian species (Harris *et al.*, 1977; Montesano & Magee, 1970).

3.3 Case reports and epidemiological studies

No data were available to the Working Group.

## 4. Summary of Data Reported and Evaluation

### 4.1 Experimental data

*N*-Nitrosodimethylamine is carcinogenic in all animal species tested: mice, rats, Syrian golden, Chinese and European hamsters, guinea-pigs, rabbits, ducks, mastomys, various fish, newts and frogs. It induces benign and malignant tumours following its administration by various routes, including ingestion and inhalation, in various organs in various species. It produces tumours, mainly of the liver, kidney and respiratory tract. It is carcinogenic following its administration prenatally and in single doses. In several studies, dose-response relationships were established.

### 4.2 Human data

No case reports or epidemiological studies were available to the Working Group. Available information on occurrence suggests that the general population may be exposed to low levels of *N*-nitrosodimethylamine; however, no exposed group suitable for an epidemiological investigation has yet been identified. Reports of relatively high levels in certain pesticide formulations and of occupational exposures that may have occurred in the manufacture and use of rocket fuels may permit the identification of exposed groups.

## 4.3 Evaluation

There is *sufficient evidence* of a carcinogenic effect of *N*-nitrosodimethylamine in many experimental animal species. Similarities in its metabolism by human and rodent tissues have been demonstrated. Although no epidemiological data were available (and efforts should be directed toward this end), *N*-nitrosodimethylamine should be regarded for practical purposes as if it were carcinogenic to humans.